

EVIDENCE-BASED CARE OF TYPE 2 DIABETES MELLITUS: EPIDEMIOLOGY, SCREENING, DIAGNOSIS AND INITIAL EVALUATION

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ABSTRACT

This three-part review article provides an overview of the evidence-based care of persons with type 2 diabetes mellitus in the view of recent literature and research work documented. Epidemiologically, type 2 diabetes is much more common and accounts for 90-95% of all diabetic cases worldwide, thus focus of this particular review is on type 2 diabetes only.

Part-I initially discusses the epidemiological overview of the disease globally and then nationally; next provides the rationale and criteria for screening and diagnosis of type 2 diabetes and summarizes the important components that should be revealed at an initial appraisal of the patient. Part-II provides key information about the non-pharmacological and pharmacological management of type 2 diabetes. Part-III reviews the prevention, screening and management of long-term complications among persons with type 2 diabetes.

KEY WORDS: *Type 2 Diabetes. Management. Evidence Based Care.*

EPIDEMIOLOGICAL OVERVIEW

A pandemic of noncommunicable diseases (NCDs) is underway in all regions of the world. This is associated with forces of globalization, with rural to urban shifts in populations, resulting with changes in diet and physical activity pattern and fueled by demographic aging. The major rise of this burden is predicted in developing countries. Overall deaths from NCDs are expected to climb from 28.1 million in year 1990 to 49.7 million by 2020, while in developing regions, by year 2020, NCDs are expected to account for seven out of every ten deaths, compared with less than half today.¹ The impact of NCDs on the lives of people is serious when measured in terms of loss of life, disablement, family hardship, poverty and economic loss.

Diabetes mellitus is one of the main diseases in this group and a major cause of premature mortality, morbidity and disability. The pandemic is growing at a rate several times that of world population growth.² Globally, the prevalence of diabetes in adults was estimated to be 4.0% (150 million) in 1995 and to rise to 5.4% (300 million) by the year 2025.³ The major part of this numerical increase will occur in developing countries. There will be a 42% increase from 51 to 72 million, in the developed countries and a 170% increase, from 84 to 228 million, in developing countries.³ Thus, by the year 2025, approximately 75% of all persons with diabetes will be living in developing countries.⁴

Pakistan is forefront in this scenario. World Health Organization (WHO) estimates that by the year 2025, the number of persons with diabetes in Pakistan will rise to 14.5 million (4.8% of world total diabetics) and Pakistan will rank 4th, as compared to 4.3 million diabetics (3.2% of the world total diabetics) at rank 8th in the year 1995,⁵ if no active intervention is made. The National Diabetes Prevalence Survey of Pakistan has shown that over 10% of people in the age group 25 years and above are diabetics and an equal number are suffering from impaired glucose tolerance. In their first two surveys, the prevalence of diabetes among adult population was found to be 13.9% in Sind, and 8.6% in Baluchistan with a further 11.1% (men) and 13.4% (women) having impaired glucose tolerance in the two provinces respectively.^{6,7} According to another survey conducted in three villages of NWFP province, the overall prevalence of diabetes and impaired glucose tolerance in both sexes was 11.1% and 9.4% respectively.⁸ Once diabetes develops, it is a costly disease to manage because of its chronic nature, severity of its complications and the means required to control them. The cost not only affects individual and his/her family, but also the health system of the country. There are substantial direct and indirect costs to society due to diabetes. Direct costs include emergency care, hospitalization, medical services, outpatient care, surgery, drugs, laboratory tests and equipment. Indirect costs include premature mortality

and loss of working days resulting in loss of production and earnings. There are also personal costs and intangibles such as pain, suffering, inconvenience and anxiety. In the United States,⁹ the estimated cost of providing care for diabetes and its complications is \$100 billion per year, with half the cost attributable to direct care. WHO estimates that for a low-income Indian family having an adult with diabetes, 25% of income will be devoted to diabetes care.¹⁰

SCREENING AND DIAGNOSIS

It is evident that persons with type 2 diabetes remain asymptomatic for longer duration of time and frequently not diagnosed until complications appear. In developed countries like United States,¹¹ 35% diabetics are unaware about their disease. The condition is expected to be even worst in less developed countries like ours. National Health Survey of Pakistan¹² documented that in Pakistan, only 36.3% of people with diabetes are aware about their condition. Undiagnosed diabetes is not a benign condition, however, and many patients have some complications by the time the disease is diagnosed. The average delay of 4 to 7 years in diagnosing type 2 diabetes translates into approximately 20% of patients having some evidence of microvascular or neurologic diabetic complications at the time of diagnosis.¹³ Among patients with undiagnosed type 2 diabetes 10% to 29% have retinopathy, 10% to 37% have proteinuria, 9% have neuropathy, 22% have abnormal heart findings and 10% have peripheral vascular disease at the time of diagnosis. In addition, about 61% have hypertension, 49% have hypercholesterolemia, and 40% have elevated low-density lipoprotein.¹⁴ In Sri Lanka,¹⁵ among persons with newly diagnosed type 2 diabetics, neuropathy was present in 25%, nephropathy in 29%, retinopathy in 15%, coronary vascular disease in 21%, stroke in 5.6% and peripheral vascular diseases in 4.8%.

In the face of these evidences, the case for diabetes screening is compelling. It is rationale and cost-effective to screen high-risk group population. However, screening of type 2 diabetes to general population is not recommended. A number of authoritative sources provide screening guidelines and each identifies a slight different group of risk factors. Recently recommended criteria¹⁶ for testing for diabetes in asymptomatic and undiagnosed adults are:

- 1) all individuals at age 45 years and above, particularly in those with a Body Mass Index (BMI) ≥ 25 [†], and, if normal, should be repeated at 3-years intervals. (* May not be correct for all ethnic groups.[‡] World Health Organization and

International Obesity Task Force recommendations for adults for the Asia-Pacific region: overweight at BMI ≥ 23 and obesity at BMI ≥ 25).

- 2) younger age or be carried out more frequently in individuals who are overweight (BMI ≥ 25), and have additional risk factors:
 - habitually physically inactive
 - have a first-degree relative with diabetes
 - belonging to certain high-risk ethnic population (African-Americans, Latino, Native Americans, Asian-Americans, Pacific Islander)
 - have delivered a baby weighting > 9 lbs or have been diagnosed with gestational diabetes mellitus
 - are hypertensive ($\geq 140/90$ mm Hg)
 - have an HDL cholesterol level ≤ 35 mg/dl (0.90 mmol/l) and/or a triglyceride level ≥ 250 mg/dl (2.82 mmol/l)
 - on previous testing had Impaired Glucose Tolerance (IGT) or Impaired Fasting Test (IFG)
 - have other clinical conditions associated with insulin resistance (e.g. PCOS or acanthosis nigricans)
 - have a history of vascular disease.

Being a rapidly emerging epidemic of type 2 diabetes in children and youth,^{17,18} persons with age < 18 years having traditional risk factors along with any of the symptom (blurred vision, dry/itchy skin, numbness/tingling in extremities, polyuria, thirst, yeast infection, unexplained weight loss) must be screened for type 2 diabetes.¹⁹

American Diabetes Association recommended three ways to diagnose diabetes in nonpregnant adults, and each must be confirmed on a subsequent day unless unequivocal symptoms of hyperglycemia are present.¹⁶ These are:

- 1) Symptoms of diabetes (classic symptoms are: polyuria, polydipsia, and unexplained weight loss) and a casual plasma glucose of ≥ 200 mg/dl (11.1 mmol/l). Casual is defined as any time of day without regard to time since last meal.
- 2) FPG ≥ 126 mg/dl (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 hours.
- 3) 2-hour PG ≥ 200 mg/dl (11.1 mmol/l) during an oral glucose tolerance test. The test should be performed using a glucose load containing the equivalent of 75 g of anhydrous glucose dissolved in water.

Hyperglycemia not sufficient to meet the criteria for diabetes is categorized as Impaired Fasting Glucose (IFG) or Impaired Glucose Tolerance IGT. However, both categories are risk factors for future diabetes and cardiovascular diseases and have been officially termed 'pre-diabetes'.¹⁶ Individuals with fasting glucose levels equal to or more than 110mg/dl (6.1 mmol/l) but less than 126 mg/l (6.9 mmol/l) are labeled as IFG and those with 2-hour plasma glucose

140 mg/dl (7.8 mmol/l) to 199 mg/dl (11.0 mmol/l) as IGT.

Although the 75-g oral glucose tolerance test (OGTT) is more sensitive and modestly more specific than fasting plasma glucose (FPG) to diagnose diabetes, it is poorly reproducible and rarely performed in practice. Because of ease of use, acceptability to patients and lower cost, the FPG is the preferred screening and diagnostic test.

INITIAL ASSESSMENT AND MANAGEMENT OBJECTIVES

Diabetes Mellitus is a complex metabolic disorder associated with large number of long-term complications. On a relative basis, people with diabetes are 25 times more likely to develop blindness and 17 times more likely to develop kidney disease than individuals without diabetes. Moreover, they are 2 to 4 times more likely to develop coronary artery disease, 2 times more likely to suffer stroke, 20 times more likely to develop gangrene and 30 to 40 times more likely to undergo a major amputation.²⁰

In addition, large number of epidemiological studies^{21,22,23} have documented the significantly higher prevalence of factors responsible for the development of long-term complications among persons with type 2 diabetes like physical inactivity, unhealthy dietary habits, smoking, overweight/obesity, hypertension and dyslipidaemia. Recently, in a multi-center study conducted in Karachi, Khuwaja AK et al²⁴ reported that among persons with type 2 diabetes, 67% were physically inactive, 68% were obese (BMI \geq 25) and 42% were hypertensive. There are, however, considerable evidences mainly including UKPDS,²⁵ HOT trial,²⁶ CARE trial,²⁷ 4S study,²⁸ suggesting that modification of risk factor results in a substantial decrease and delay in the development of diabetic complications, disabilities and premature mortality.

Thus, standard management of type 2 diabetes not only considers lowering the blood glucose level but should also focus on the correction and modification of any associated risk factor and complication. Careful appraisal and evaluation on initial visit plays a vital role in this regard. This evaluation is mainly comprised of a detailed medical history, thorough physical examination and rationale laboratory evaluation.

Essential elements that should be covered in history of patient with type 2 diabetes at the initial visit include: assessment of symptoms of diabetes and its complications, inquiry about risk factors for diabetes and its complications (eating pattern, exercise history, smoking, hypertension, dyslipidemia), family history of diabetes, history of gestational diabetes or delivery of a baby weighting > 9 lbs, history of other disease and drugs that may be associated with hyperglycemia,

history of current and repetitive infection (like tuberculosis, skin, soft tissue, foot, dental, and genitourinary infections). Lifestyle, psychosocial, cultural, educational and economic factors that might influence the management of diabetes should be asked. In addition, if person is already on diabetes therapy, be inquired about previous treatment programs, management compliance, results of the previous laboratory test, prior glycemic control, diabetes-related knowledge and self-care training. Physical examination at initial visit should include height, weight and blood pressure measurement, evaluation of pulses (carotid, femoral, popliteal, posterior tibialis, and dorsalis pedis), cardiac examination, neurological examination, ophthalmoscopic examination (preferably with dilated fundi), oral examination and foot examination (including sensation of the 5.07 monofilament). At initial visit, patient with type 2 diabetes should also be evaluated for fasting plasma glucose level, glycohemoglobin, fasting lipid profile (total cholesterol, HDL, LDL and triglyceride), serum creatinine, resting electrocardiogram and urine analysis (glucose, ketones, proteins, sediments).

Recommended target levels for management of persons with type 2 diabetes are¹⁶:

- Glycemic control
 - A1C < 7.0%
 - Preprandial plasma glucose 90-130mg/dl (5.0 -7.2mmol/l)
 - Peak postprandial plasma glucose < 180 mg/dl (< 10.0 mmol/l)
- Blood pressure < 130/80 mmHg
- Lipids
 - LDL < 100 mg/dl (< 2.6 mmol/l)
 - Triglycerides < 150 mg/dl (< 1.7 mmol/l)
 - HDL > 40 mg/dl (> 1.1 mmol/l)

Setting of management plan and goals should be formulated as an individualized therapeutic alliance among the patient, his/her family and the physician. In developing the plan, consideration should be given to the patient's age, type of personality, nature of work schedule, habitual physical activity (including leisure time activity), eating patterns, social and cultural factors and presence or absence of diabetic complications and other co-morbidities.

At the initial visit, the general objectives of diabetes management should also be discussed with patient and their families. Glycemia control is a fundamental to the management of diabetes, however, other objectives should include to relieve symptoms, to correct associated health problems, to reduce morbidity, mortality and economic costs of diabetes, to prevent/delay the complications and to monitor the

development of such complications and provide timely intervention. Thus, to improve the quality of life and productivity of the individual with diabetes.²⁹ Moreover, regular visits should be scheduled for all persons with type 2 diabetes, to establish and monitor treatment goals and to achieve metabolic control.

Without appropriate education of persons with diabetes regarding its care, the desired therapy objectives are difficult or even impossible to meet. Education of person with diabetes and his/her family is the cornerstone for its management. People with diabetes should be taught about the self-care of the disease and encouraged to participate in managing and monitoring of their condition. This intervention should be initiated at initial visit followed by subsequent re-enforcement in follow-up visits.

CONCLUSION

As a result of population aging, industrialization and urbanization with lifestyle and dietary changes, the burden of noncommunicable diseases including diabetes is emerging as a clinical and public health challenge throughout the world. Pakistan is already facing a high burden of diabetes and by the year 2025, the number of persons with diabetes in Pakistan will rise to 14.5 million and it will be ranked 4th globally in terms of diabetes burden.

Type 2 diabetes is a progressive and degenerative disease in nature, remains asymptomatic for long duration of time in majority of cases. If screening and diagnosis is not done when required, it leads to a large number of complications with devastating effects on the person with diabetes, their families and health system of the country in terms of direct and indirect cost. Type 2 diabetes is a complex metabolic abnormality that involves virtually every organ of the body and its management is a labor-intensive process that requires continuing quality medical care. Management of type 2 diabetes not only considers lowering of blood glucose level but should also focus on the correction and modification of associated factors, thus, to prevent/delay the long-term complications. Patient's education regarding the risk factors, complications, treatment objectives and compliance is the cornerstone of diabetes management.

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REFERENCES

1. Christopher JL, Alan D. Global Burden of Disease (Summary) Harvard University Press 1996.
2. White F, Rafique G. Diabetes prevalence and projections in south Asia: An emerging public health priority for the 21st century. (Proceeding from the ninth international congress). World Federation of Public Health Associations. Beijing, China. 2-6 September 2000.
3. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. *Diabetes Care*. 1998; 21(9): 1414-31
4. King H. WHO and International Diabetes Federation: regional partners (Editorial). *Bull World Health Organ*. 1999; 77(12): 954
5. Press Release WHO/63 14th September 1998. <http://www.who.int/inf-pr-1998/en/pr98-63.html>
6. Shera SA, Rafique G, Khuwaja IA et al. Pakistan National Diabetic Survey: Prevalence of glucose intolerance and associated factors in Shikarpur, Sindh Province. *Diabet Med*. 1995; 12: 1116-21
7. Shera AS, Rafique G, Ahmed KI et al. Pakistan National Diabetes Survey: prevalence of glucose intolerance and associated factors in Baluchistan Province. *Diabetes Res Clin Pract*. 1999; 44: 49-58
8. Shera SA, Rafique G, Ahmed KI et al. Pakistan National Health Survey: Prevalence of glucose intolerance and associated factors in North West Frontier Province (NWFP) of Pakistan. *J Pak Med Assoc*. 1999; 49(9): 206-10
9. Harris MI, Eastman RC. Early detection of undiagnosed non-insulin-dependent diabetes mellitus. (Editorial) *JAMA*. 1996; 276(15): 1261-2
10. World Health Organization. Fact Sheet No. 236. 1999 <http://www.who.int/inf-fs/en/fact236>
11. Harris MI, Flegal KM, Cowie CC et al. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The third national health and nutrition examination survey 1988-1994. *Diabetes Care*. 1998; 21(4): 518-24
12. Pakistan Medical Research Council. National Health Survey of Pakistan 1990-94. Islamabad, Pakistan. Network Publication Services, 1998
13. United Kingdom Prospective Diabetes Study Group (UKPDS 6). Complications with newly diagnosed type 2 diabetic patient and their association with different clinical and biochemical risk factors. *Diabetes Res*. 1990; 13: 1-11
14. Harris MI. Undiagnosed NIDDM: clinical and public health issue. *Diabetes Care*. 1993; 16(4): 642-52

15. Weerasuriya N, Siribaddana S, Dissanayake A et al. Long-term complications in newly diagnosed Sri Lankan patients with type 2 diabetes mellitus. *QJMed*. 1998; 91:439-43
16. American Diabetes Association. Standards of medical care for patients with diabetes mellitus. *Diabetes Care*. 2003; 26 (suppl): S33-50
17. Rocchini AP. Childhood obesity and a diabetes epidemic (editorial). *N Engl J Med* 2000; 346(11): 854 – 55
18. Rosenbloom AL, Young RS, Joe JR et al. Emerging epidemic of type 2 diabetes in youth. *Diabetes Care*. 1999; 22: 345 – 54
19. Staged Diabetes Management. Decision-paths 2nd ed. International Diabetes Center, Institute for research and education, Minneapolis, USA, 1998
20. Davidson MB. Diabetes Mellitus: Diagnosis and treatment. 4th ed. California. 1998: 267
21. Multiple Risk Factors Intervention Trial Research Group: Diabetes, other risk factors, and 12 year cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. *Diabetes Care* 1993; 16:434-44
22. Williamson DE, Thompson TJ, Thun M et al. Intentional weight loss and mortality among overweight individuals with diabetes. *Diabetes Care* 2000; 23:1499-504
23. Wannamettee SG, Shaper AG, Alberti KG. Physical activity, metabolic factors, and the incidence of coronary heart diseases and type 2 diabetes. *Arch Intern Med* 2000; 160:2108-16
24. Khuwaja AK, Rafique G, Franklin W. Macrovascular complications and their associated factors among persons with type 2 diabetes in Karachi – A multi-center study (In press).
25. United Kingdom Prospective Diabetes Study Group (UKPDS 38). Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes. *BMJ* 1998; 317:703-13
26. Hansson L, Zanchetti A, Carruthers SG et al. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomized trial. *Lancet* 1998; 351: 1755-62
27. Golderg RB, Mellies MJ, Sacks FM et al. Cardiovascular events and their reduction with pravastatin in diabetic and glucose-intolerance myocardial infarction survivors with average cholesterol levels: subgroup analyses in the Cholesterol and Recurrent Event (CARE) trial. *Circulation* 1998; 98: 2513-9
28. Pyorala K, Pedersen TR, Kjekshu J et al. Cholesterol lowering with simvastatin improves prognosis of diabetic patients with coronary artery disease: a subgroup analysis of the Scandinavian Simvastatin Survival Study (4S). *Diabetes Care* 1997; 20: 614-20
29. World Health Organization. Management of diabetes mellitus: standards of care and clinical practice guidelines. WHO regional office for Eastern Mediterranean Alexandria, Egypt 1994

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